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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,434	03/15/2001	Glenn McGall	2719.2017-001	6484

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EXAMINER

EPPS FORD, JANET L

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM-
Advisory Action

Application No.

09/810,434

Applicant(s)

MCGALL ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 26 May 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) ☐ they raise the issue of new matter (see Note below);
 - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

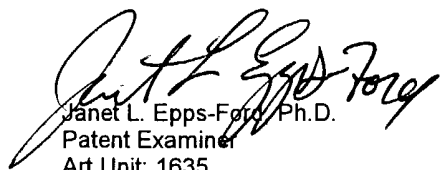
Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: _____

Claim(s) withdrawn from consideration: _____

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5-26-04.
10. ☐ Other: _____


Janet L. Epps-Ford, Ph.D.
Patent Examiner
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DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. In the Final Office Action mailed 12-19-03 the examiner indicated that claims 4, and 14-17 were indicated as allowable over the prior art. However, the examiner also indicated that these claims were rejected under 35 USC 112, 2nd paragraph.

Claim Rejections - 35 USC § 103

3. Claims 1-3, 5-13 and 18-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Earhart et al. in view of McGall et al., for the reasons of record set forth in the Official Action mailed 5-28-03.

Applicant's arguments filed 5-26-04 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the examiner has based the instant rejection upon incorrect assumptions regarding the claimed invention. According to Applicants one skilled in the art would not expect to see a direct correlation between iodine concentration and hybridization signal intensity. According to Applicants, prior to the instant invention, one would have expected a monotonic decrease in functional performance in nucleic acid array as the iodine concentration decreased, due to incomplete oxidation of the array; they would have expected functional performance to reach an asymptote as iodine concentration increased, and furthermore once skilled in the art would not have expected functional performance to decrease at higher iodine concentrations (*e.g.* at 0.1 M). First, it is noted that Applicants provide no reference to support their conclusions as to what one of skill in the art would have expected, prior to the filing of the current application. Applicant's arguments do not

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take the place of evidence that since the prior art disclosed the general conditions regarding the use of iodine as an oxidizing agent to convert a phosphite ester linkage to a phosphate, it would not have been obvious to optimize the general conditions to maximize experimental results. Applicants have merely discovered the concentration of iodine, in particular 0.02 M wherein hybridization intensity, as an indicator of functional performance, is optimized. As stated previously, the unexpected results in regards to the hybridization intensities associated with using iodine concentrations of about 0.005 M to about 0.05 M iodine was not demonstrated by the McGall Declaration. For example, see Experiment 1 and 2, page 5 of the McGall Declaration. In both experiments, hybridization intensity decreased at 0.01 M iodine with respect to that observed at 0.02 M iodine. There is no direct evidence that would lead the skilled artisan to expect that at a concentration lower than 0.01 M iodine, i.e. from about 0.005 M up to 0.01 M would produce an average hybridization intensity greater than that observed at 0.10 M or greater concentrations of iodine used in the prior art. Based upon the data provided in the McGall declaration the ordinary skilled artisan would expect that using concentrations lower than 0.01 M would produce hybridization intensities that are lower than that observed at 0.1 M iodine. The experimental data set forth in the declaration of McGall is not commensurate in scope with the instantly claimed invention, particularly wherein the claims recite an iodine concentration range of 0.005 M to about 0.05 M iodine.

In the oxidizing agent study provided by Applicants on 5-26-04, Applicants indicated that the standard deviation of the hybridization intensities for the two experiments at 0.10 M iodine was 56. Based upon, this information the values observed using a concentration of 0.10 M iodine in the claimed methods would not be considered statistically different from those

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observed using 0.01 M, or 0.05M. Moreover, the study did not provide the standard deviation values for the experiments performed at 0.01 M, 0.02 M or 0.05 M, therefore no clear conclusion can be drawn from the data presented in this table. On page 4 of Applicant's response filed 5-26-04, Applicants disagree with the Examiner's position that the hybridization intensities from nucleic acid arrays prepared using the claimed concentrations of iodine are not considered to be statistically different. Applicants normalized the data produced by Applicants in the McGall Declaration by taking the 0.1 M hybridization intensity as 100% in the two experiments. As stated previously there is definitely a significant difference between the use of 0.1 M iodine and 0.02 M iodine. However, there is no data regarding iodine concentrations lower than 0.01 M iodine, and there is no evidence to support increased hybridization intensities for the full scope of the claimed range of "about 0.005 M to about 0.05 M iodine."

Furthermore, since the specification as filed does not provide a clear definition of the term "about" as recited in the claimed ranges, the metes and bounds of the range "from about 0.005M to about 0.05M," is unclear. The McGall Declaration does not provide any evidence that concentrations that are "about 0.005" or "about 0.01 M" would produce unexpected results when practicing the claimed method. At best, it appears that the McGall Declaration provides unexpectedly higher hybridization intensity values for only one concentration of iodine, namely 0.02 M.

Claim Rejections - 35 USC § 112

4. Claim 18 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (New Matter Rejection), for the reasons of record set forth in the Official Action mailed 12-19-03.

Applicant's arguments filed 5-26-04 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the range recited in claim 18, namely "from about 0.01M to about 0.05M" clearly comply with the description requirement. Applicants refer to MPEP § 2163.05 as support for their amendment. However, unlike the situation set forth in this section of the MPEP the specific example of the limitation "36%" provided support for the amendment "between 35% and 60," the example given in the MPEP did not provide support for a range "from about 35%," as compared to the instant case wherein the limitation "from about 0.01M" is 2 fold lower than 0.02M and clearly includes ranges less than 0.01M. Moreover, since the term "about" is not adequately described in the specification as filed, the phrase "from about 0.01M" may encompass ranges beyond that of 0.05M or less than 0.02 M. It is unclear how the disclosure of 0.02M would inherently disclose ranges that are two-fold less than 0.02M, therefore the range "from about 0.01M to about 0.05M," can not be considered to comply with the written description requirement.

As stated in the prior Office Action, the limitation, "from about 0.01M to about 0.05M," is considered new matter since one of skill in the art would not consider this limitation to be inherently supported by the discussion in the original disclosure. See MPEP § 2163.06, which states "The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement."

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Applicants must remove the new matter set forth in claim 18 in response to this Office Action.

5. Claims 1-19 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record set forth in the Official Action mailed 12-19-03.

6. Applicant's arguments filed 5-26-04 have been fully considered but they are not persuasive. Applicants disagree with the Examiner's characterization of *WL Gore & Associates*, and traverse on the grounds that because preparing solutions containing a particular concentration of a substance and determining concentrations is so well known in the art (particularly when the substance is iodine), there is no need for either the specification or the prosecution to provide additional disclosure on the meaning of "about" as it relates to the concentration of iodine. Contrary to Applicant's assertions, because preparing iodine solutions containing a particular concentration is so well known in the art, there should be no ambiguity or impreciseness associated with iodine concentration determination. There is no analogy seen here as compared to the measurement of time with a stopwatch. The facts set forth in the *W.L. Gore & Associates* case do not specifically correlate with the current facts of the instant application since there is nothing in the specification, prosecution or the prior art to provide any indication as to what range of specific activity (i.e. utility in regards to oxidization of a phosphite ester to a phosphate) is covered by the term "about." The prior art shows that ranges that are 2 times greater than the upper limit of Applicant's range are expected to possess activity. However, it is unclear what other concentrations of iodine would also possess the ability to oxidize a phosphite

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ester linkage to a phosphate ester linkage. Therefore, since Applicant's have not defined the range of iodine concentration that is covered by the term "about" as used in the context of the instant claims, the ordinarily skilled artisan would not be able to determine the full scope of iodine concentrations that are encompassed by the range "from about 0.005 M to about 0.05 M."

Although, Applicants may argue that the specifics of the instant application are analogous to that associated with *W. L. Gore & Associates*, Applicant's arguments do not provide a clear and precise definition of the term "about" such that the skilled artisan would be reasonably apprised of the full scope of the claimed invention. However, Applicants do not address the fact that the court also held that claims reciting "at least about" were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term "about." *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d (1200, 18 USPQ2d 1016 (Fed. Cir. 1991).

Moreover, according to MPEP § 2173.05(a) [R-1] "The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed. Applicants need not confine themselves to the terminology used in the prior art, but are required to make clear and precise the terms that are used to define the invention whereby the metes and bounds of the claimed invention can be ascertained. During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification."

Applicant's arguments are not persuasive. The instant claims remain rejected for the reasons of record.

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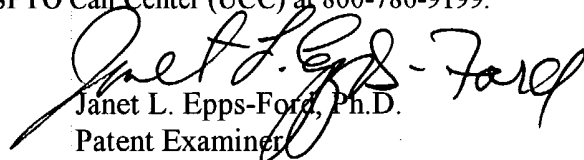
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Janet L. Epps-Ford, Ph.D.
Patent Examiner
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JLE